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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,107	03/31/2004	Mangala Gowri Ponnappalli	U 015131-4	6583
7590 LADAS & PARRY 26 WEST 61ST STREET NEW YORK, NY 10023				
09/11/2009				
EXAMINER				
MCCORMICK, MELENIE LEE				
ART UNIT		PAPER NUMBER		
1655				
MAIL DATE		DELIVERY MODE		
09/11/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/815,107

**Applicant(s)**

PONNAPALLI ET AL.

**Examiner**

MELENIE MCCORMICK

**Art Unit**

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 7, 9-12 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 15-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 9-11, 14 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/808)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 August 2009 has been entered.

Claims 1-5, 7, 9-12, and 14-20 are pending.

Claims 12 and 15-19 stand withdrawn from consideration.

Claims 1-5, 7, 9-11, 14 and 20 are presented for examination on the merits.

### ***New Rejections***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 9-11, 14 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites 'imperatorin having a high degree of purity' in step h). A 'high degree of purity' is a relative term. The instant specification does not provide a means

for evaluating what is or is not encompassed by the term 'high'. This phrase therefore renders the claim indefinite because the metes and bounds of the claim cannot be determined.

### ***Maintained Rejections***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1- 5, 7, and 9-11 and 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saha et al. (1957) in view of Bastnet et al. (2001) and in view of Bizhanova et al. (1977) for the reasons set forth in the previous Office Action, which are discussed below.

Saha et al. beneficially teach a method of isolating imperatorin which comprises the steps of extracting fruit pulp of *Angle marmelos* with alcohol under reduced pressure (which would concentrate the alcoholic extract ), and then freeing the extracted pulp from alcohol under reduced pressure and soxhletting with benzene ( the step of freeing the extract from alcohol and then extracting in another solvent would to 'partition' the extract from the alcohol to the benzene, which would necessarily reduce the volume of the alcohol extract). Saha et al. further teaches that the extract is then dried over anhydrous sodium sulfate and concentrated (thus the solvent would be removed). Saha

further teaches that the extract is then crystallized in ethanol (see e.g. 229 –isolation of Alloimperatorin). Saha et al also teaches that the mother liquid left over after the crystallization is then chromatographed over a column of alumina and then eluted with benzene and crystallized with petroleum ether. It is further disclosed that this elution and crystallization is repeated and multiple fractions are collected. (see e.g. page 229- Isolation of Imperatorin).

Saha et al. do not explicitly teach that a halogenated solvent is used or that a silica gel column is used.

Bastnet et al. beneficially teach that imperatorin is found in the chloroform soluble fraction of a methanolic extract of a plant (see e.g. abstract).

Bizhanova et al. beneficially teach that imperatorin can be isolated after alcoholic extraction using a silica gel column (see .g. English Abstract).

It would have been obvious to one of ordinary skill in the art to optionally select another non-polar solvent besides the benzene used by Saha in the method of isolating imperatorin taught by Saha. A person of ordinary skill in the art at the time the claimed invention was made would have had a reasonable expectation of success in substituting chloroform for the benzene taught by Saha because Bastnet discloses that imperatorin is soluble in chloroform. Thus, a person of ordinary skill in the art would have a reasonable expectation of success in isolating imperatorin using chloroform. A person of ordinary skill in the art would have also had a reasonable expectation of success in using silica gel column chromatography instead of alumina since Bizhanova et al. also teach teaches that after an alcoholic extraction, imperatorin can be separated using

silica gel. The particular mesh size would be routine experimentation since the compound being isolated (imperatorin) is known. Although the filtration step instantly claimed in steps e and f of claim 1 is not explicitly taught by Saha et al., the removal of the crystals from the 'mother liquid' would suggest to one of ordinary skill in the art that filtrations must have taken place. Although the particular type of fruit pulp (i.e. immature/mature or dry/fresh) is not explicitly taught, a person of ordinary skill in the art would have a reasonable expectation of success in using what is readily available, which would inevitably be one of the instantly claimed types of *Angle marmelos*. It is also considered routine experimentation to optimize the time which is spent on extraction and the particular pulp to solvent ratio depending upon the yield of imperatorin which is desired. Although the particular yield of imperatorin after the soxhletting step taught by Saha is not explicitly taught and the amount of time spent soxhletting is not taught, a person of ordinary skill in the art would have a reasonable expectation of success in optionally adjusting the amount of time spent during any step in the extraction process in order to improve the yield of the desired product.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***New Rejections***

Claims 1- 5, 7, and 9-11 , 14 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saha et al. (1957) in view of Bastnet et al. (2001) in view of Bizhanova et al. (1977) and in view of Maksyutina et al. (1966).

Saha et al. Bastnet et al. and Bizhanova et al. render obvious a method of isolating imperatorin from Aegle marmelos fruit and are relied upon for the reasons set forth above.

Saha et al. Bastnet et al. and Bizhanova et al. do not explicitly teach the method wherein step a) is effected in a Soxhlet apparatus for 6-12 hours with ethylenedichloride.

Maksyutina et al. at teach that seeds of parsnip are extracted with ethanol and then dichloroethane. The dicloroethane extract is fractionated onto a column and imperatorin is eluted (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use ethylenedichloride (dichloroethane) as an extraction solvent instead of alcohol. A person of ordinary skill in the art would have recognized this as an alternative option because it is clear from the disclosure of Maksyutina et al. that imperatorin is soluble in both alcohol and dichloroethane. A person of ordinary skill in the art would have reasonably understood from the disclosure of Saha et al. that the first extraction under pressure with alcohol is meant to concentrate the extract. Therefore, it would be within the level or ordinary skill in the art to concentrate the first extract using another method, for example, soxhletting. Because Saha et al. disclose the use of soxhletting in other method steps, this was a known

method of extraction at the time of the invention. Therefore, a person of ordinary skill in the art would have had a reasonable expectation of success in using a known extraction method to extract imperatorin into a solvent it is known to be soluble in. As discussed above, the amount of time soxhletting is performed would be adjustable in order to optimize yield. In addition, as discussed above, the use of Aegle marmelos fruits in various stages of development would be dependent upon what is readily available and would therefore determine the yield of imperatorin from fruits at each stage of development.

### ***Response to Arguments***

Applicants argue that the substitution of chloroform for benzene in the method disclosed by Saha et al. would not have been obvious. Applicants argue that furanocoumarins such as imperatorin are often found in combination with other compounds, from which their separation is difficult. Applicants argue that the use of polar solvents for extraction results in extracts having a high amount of color and fatty material which must be removed to produce a pure product. Applicants argue that chloroform is more polar than benzene. This is not denied. A person of ordinary skill in the art would have been motivated to use chloroform in the method claimed instead of benzene because the desired compound (imperatorin) was known at the time of the invention to be soluble in chloroform. Therefore a person of ordinary skill in the art would have had a reasonable expectation of success in using chloroform. It would have



been an option available to the artisan at the time of the invention because the compound of interest was known to be soluble in chloroform. Therefore the substitution of this solvent for the benzene used by Saha et al. would have been obvious.

Applicants argue that benzene has a dielectric constant of 2.3 and chloroform has a dielectric constant of 4.8 and that when one is seeking to move away from polar solvents, one would not move to a more polar solvent. It is not clear why Applicants are asserting that there was a desire to move away from polar solvents. Applicants also argue that the solubility of a compound is only one factor considered when looking for a suitable solvent to use in an extraction process. Applicants argue that other factors include the solubility of other materials in the solvent and the density of the solvent. Applicants argue that the density of benzene is less than chloroform and this is another reason why a person of skill in the art would not choose to use chloroform. A person of skill in the art, however, does not need multiple reasons to make the substitution. One reason would be enough to render the substitution obvious. The reason has already been discussed (the known solubility of imperatorin in chloroform). In addition, Applicants motivation for combining does not have to be the same as that of the prior art. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In addition, Applicants have not disclosed why the density of the solvent would be critical or why it would appear to a person of skill in the art that using a more dense solvent would be detrimental or non-

advantageous. Likewise, Applicants have not disclosed why it would be apparent to one of skill in the art that the art to move away from more polar solvents in order to extract imperatorin. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

The rejection is therefore deemed proper and is maintained.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELENIE MCCORMICK whose telephone number is (571)272-8037. The examiner can normally be reached on M-F 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia Leith/  
Primary Examiner, Art Unit 1655  
For MM 9/10/2009